ASCO 2021 REVIEW AND UPDATES

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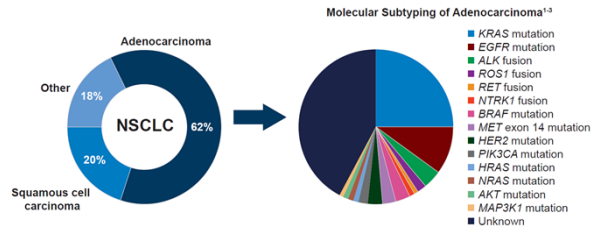
GW ONCOLOGY UPDATE

Disclosures

- Consulting
  - AstraZeneca, BMS, Janssen, Merck, Takeda, Novartis, Genentech, Eli Lilly, Daiichi Sankyo, Turning Point
- Research Support
  - AstraZeneca, Daiichi Sankyo, Calithera, Genentech, Turning Point

GW ONCOLOGY UPDATE 2

Oncogenic Mutations in NSCLC



1. NCCN Clinical Practice Guidelines in Oncology. Non–Small Cell Lung Cancer. Version 5.2020. https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf.
2. Lindeman NI et al. *J Thorac Oncol.* 2018;13:323-358. 3. Kalemkerian GP et al. *J Clin Oncol.* 2018;36:911-919.

GW ONCOLOGY UPDATE 3

EGFR RESISTANCE STRATEGIES

GW ONCOLOGY UPDATE 4

FLAURA: Frontline Osimertinib[1]

Phase 3 study of osimertinib vs standard-of-care EGFR TKI as first-line treatment for *EGFR* mutation–positive, locally advanced, or metastatic NSCLC

- Advanced *EGFR*-mutated NSCLC
- N = 650

R

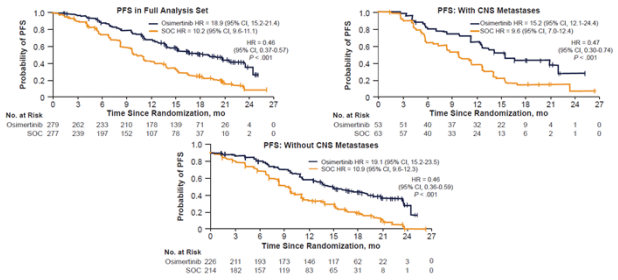
- Osimertinib
- Erlotinib or gefitinib

Primary endpoint: PFS
Key secondary endpoints: ORR, OS, and QoL

1. https://clinicaltrials.gov/ct2/show/NCT02296125.

GW ONCOLOGY UPDATE 5

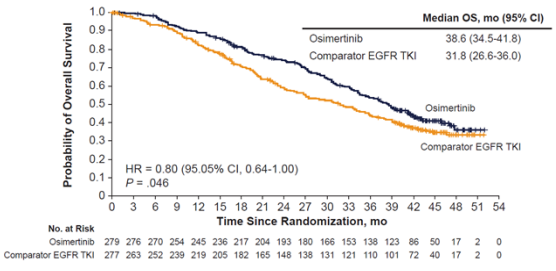
FLAURA: Osimertinib PFS[1]



1. https://clinicaltrials.gov/ct2/show/NCT02296125.

GW ONCOLOGY UPDATE 6

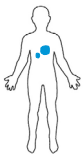
FLAURA: Osimertinib OS[1]



1. Ramalingam SS et al. *N Engl J Med.* 2020;382:41-50.

GW ONCOLOGY UPDATE 7

Treatment Paradigm for *EGFR*-Mutant Lung Cancer[1]



TKI-Naïve *EGFR*-mutant tumor

Osimertinib

PFS ~19 months
Response Rate ~80%

Resistance

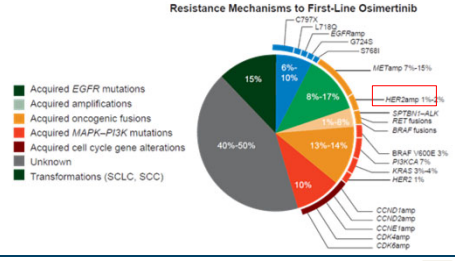
1. Soria JC et al. *N Engl J Med.* 2018;378:113-125.

GW ONCOLOGY UPDATE 8

Acquired Drug Resistance: Osimertinib[1]

First-line osimertinib is still relatively new, and we are still learning the resistance mechanisms

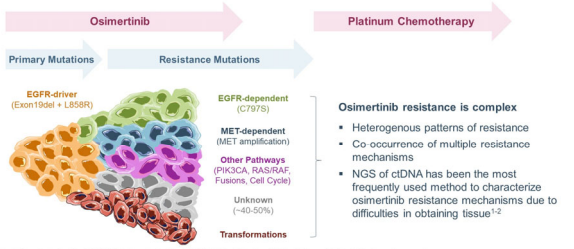
Resistance Mechanisms to First-Line Osimertinib



1. Leonetti A et al. *Br J Cancer.* 2019;121:725-737.

GW ONCOLOGY UPDATE 9

Acquired Resistance to Osimertinib in EGFRm NSCLC



Osimertinib resistance is complex

- Heterogenous patterns of resistance
- Co-occurrence of multiple resistance mechanisms
- NGS of ctDNA has been the most frequently used method to characterize osimertinib resistance mechanisms due to difficulties in obtaining tissue[1-2]

[1]Papadimitrakopoulou. *Annals of Oncol* 29:VIII741. [2]Ramalingam. *Annals of Oncol* 29:VIII740. ctDNA, circulating tumor DNA; Exon19del, exon 19 deletion; NGS, next generation sequencing.

10

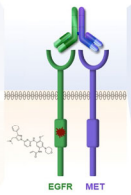
Amivantamab and Lazertinib

Amivantamab (am-e-van-tuh-mab)

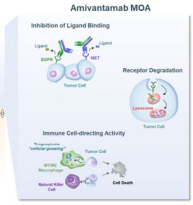
- Fully human bispecific antibody that targets EGFR and MET
- Fc portion has immune cell-directing activity[1]
- Demonstrated clinical activity across diverse EGFRm NSCLC[2-4]
- Granted Breakthrough Therapy Designation for EGFRm Exon20ins NSCLC post-chemotherapy in US and China

Lazertinib (la-zer-tin-ib)

- Potent 3rd-gen TKI with efficacy in activating EGFR mutations, T790M, and CNS disease[5,6]
- Low rates of EGFR-related toxicity such as rash and diarrhea[5]
- Low cardiovascular safety risk[7]
- Safety profile that supports combination with other anti-EGFR molecules



Amivantamab MOA



[1]Vijayaraghavan. *Mol Cancer Ther* 19:2044. [2]Haura. *JCO* 37:9009 (oral). [3]Park. *JCO* 38:9512 (poster). [4]Sabari. *JTO* 16:S106 (oral). [5]Ahn. *Lancet Oncol* 20:P1691. [6]Kim. *JCO* 38:9571 (poster). [7]Haddish-Berhane. *JTO* 16:S877 (poster). BTD, Breakthrough Therapy Designation; CNS, central nervous system; EGFRm, epidermal growth factor receptor mutant; gen, generation; MOA, mechanism of action; NSCLC, non-small cell lung cancer; TKI, tyrosine kinase inhibitor

11

CHRYSALIS Phase 1 Study Design: Combination Cohort (NCT02609776)

Key Objectives

- Establish RP2CD
- Safety and efficacy at RP2CD

Key Eligibility Criteria

- Metastatic/unresectable NSCLC
- Measurable disease (expansion cohort)
- EGFR Exon19del or L858R mutation

Biomarker Analysis[9]

- NGS of pretreatment tumor biopsy and ctDNA collected prospectively
- IHC for EGFR/MET expression

This presentation provides updated results with longer follow-up from the ESMO 2020 oral presentation (Cho *Ann Oncol* 31 S813 Oral #12500). [9]1 alteration detected in 42/44 ctDNA and 29/45 tumor NGS analyses. C, cycle; EGFR, epidermal growth factor receptor; IHC, immunohistochemistry; QW, weekly; Q2W, every 2 weeks; RP2CD, recommended phase 2 combination dose

12

Demographics and Baseline Disease Characteristics

	Total (N=45)
Median age, years (range)	65 (39–85)
Male / Female, n (%)	20 (44) / 25 (56)
Race, n (%)	
Asian	19 (42)
White	20 (44)
Black	2 (4)
Not reported / multiple	4 (1)
Smoking history	
Non-smoker	20 (44)
Smoker	25 (56)

	Total (N=45)
Previously reported brain metastases, n (%)	13 (29)
Median prior lines, n (range)	2 (1–4)
Prior 1st or 2nd-gen TKI, n (%)	33 (73)
Prior 3rd-gen TKI, n (%)	45 (100)
EGFR primary mutation, n (%)	
Exon 19 deletion	30 (67)
Exon 21 L858R	14 (31)
Unknown[a]	1 (2)

[a]Based on local testing, central testing identified Exon 19 deletion

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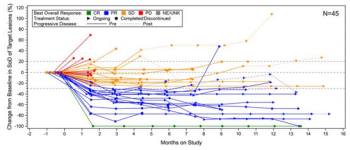
13

Durable Responses Observed with Amivantamab + Lazertinib with Manageable Safety



Investigator-assessed Response (N=45)	
mF/U: 11.0 months (range, 1.0–15.0)	
mDOT: 5.6 months (range, 0.5–14.8)	
ORR	36% (95% CI, 22–51)
mDOR, months	9.6 (95% CI, 5.3–NR)
DOR ≥6 months	69%
CBR	64% (95% CI, 49–78)
mPFS, months	4.9 (95% CI, 3.7–9.5)

- Safety profile consistent with previous experience with amivantamab + lazertinib[1]
- Most common AEs were IRR (78%), rash (acneiform dermatitis, 51% + rash, 27%), and paronychia (49%)
  - Majority were grade 1–2
- Treatment-related: grade ≥3 AE (16%), discontinuations (4%), dose reductions (18%)

19 Apr 2021 clinical cutoff. Four patients did not have postbaseline disease assessments and are not included in the plot. [1]Cho. Ann Oncol 31:S815. Oral #12560.
AE, adverse event; CBR, clinical benefit rate (CR, PR, or SD ≥11 weeks); CR, complete response; IRR, infusion-related reaction; mDOR, median duration of response; mDOT, median duration of treatment; mF/U, median follow-up; mPFS, median progression-free survival; NE, not evaluable; NR, not reached; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease; SoD, sum of target lesion diameters; UNK, unknown

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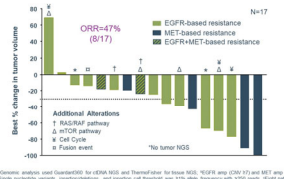
14

Response Among Patients with Identified EDFR/MET-based Resistance

- 17 of 45 patients were identified with either EGFR/MET-based resistance by NGS[a] (ctDNA/tissue)
- ORR in this subgroup was 47%, mDOR was 10.4 months, CBR was 82%, and mPFS was 6.7 months



Resistance[b]	Alterations[c]	
EGFR-based	C797S (n=7) Amp (n=3) L718X (n=3) G724S (n=2)	L792H (n=1) G796S (n=1) E709K (n=1)
MET-based	Amp (n=5)	METex14 (n=1)
Additional	PIK3CA E542X (n=2) CCNE1 Amp (n=1) PIK3CA Amp (n=1) CCND1 Amp (n=1) CDK4 (n=1)	KRAS Amp (n=1) FGFR3-TACC3 fusion (n=1) KRAS G12D (n=1) CDKN2A G101W (n=1)

[a]Genomic analysis used GuardantOMNI for ctDNA NGS and ThermoFisher for tissue NGS. [b]EGFR amp (CNV ≥7) and MET amp (CNV ≥3) were based on tumor NGS; other amps were based on tumor NGS (CNV ≥7) or ctDNA NGS (CNV ≥3). Single nucleotide variants, insertion/deletions, and insertion call threshold was ≥1% allele frequency with ≥250 reads. [c]Eight patients had ≥1 alteration. Amp, amplification; CNV, copy number variation

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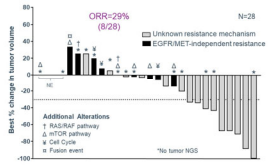
15

Response Among Patients without Identified EDFR/MET-based Resistance

- Among the remaining 28 patients who did not have an identified EGFR/MET-based resistance by NGS[a], the ORR was 29%, mDOR was 8.3 months, CBR was 54%, and mPFS was 4.1 months
- All 8 responders in those without identified EGFR/MET-based resistance were unknown resistance by NGS

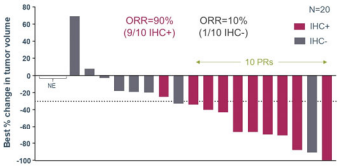


Resistance	Alterations[b]
EGFR/MET-independent	PIK3CA E545K (n=3) CCND1 Amp (n=2) CCND2 Amp (n=1) KRAS A18V (n=1) KRAS G12C (n=1) PIK3CA H1047R (n=1) PTEN I33del (n=1) PTEN N48K (n=1) SQSTM1-ALK fusion (n=1)
Not identified (n=18)	

[a]Genomic analysis used GuardantOMO for cfDNA NGS and ThermoFisher for tissue NGS. [b]Two patients had ≥1 alteration. NE, not evaluable (no postbaseline assessment for 4 patients)

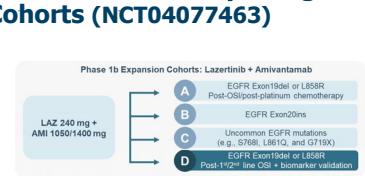
Response Among Patients with EDFR/MET Expression by IHC Staining

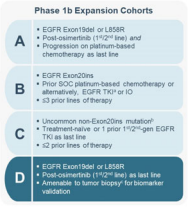
- 20/45 had tumor biopsy sufficient for IHC staining after tumor NGS
- 10 were IHC+ for EGFR/MET (combined EGFR+MET H score ≥400), with remainder defined as IHC-
- IHC+ patients had ORR of 90%, mDOR of 9.7 months, CBR of 100%, and mPFS of 12.5 months



IHC, immunohistochemistry; NE, not evaluable (no postbaseline assessment for 2 patients)

CHRYSALIS-2 Study Design: Phase 1b Expansion Cohorts (NCT04077463)





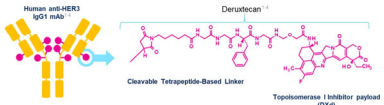
[a]Includes investigational EGFR TKI targeting Exon20ins (e.g., mobocertinib and poziotinib). [b]e.g., S768I, L861Q, G719X. [c]After progression on most recent system treatment or from initial biopsy in metastatic setting.
AMI, amivantamab; Exon20ins, exon 20 insertion; IO, immuno-oncology therapy; LAZ, lazertinib; OSI, osimertinib; SOC, standard of care

Patritumab Deruxtecan (HER3-DXd)—Targeting HER3 May Address Multiple EGFR TKI Resistance Mechanisms

- HER3-DXd is an ADC with 3 components:[1,2]
  - A fully human anti-HER3 IgG1 mAb (patritumab), covalently linked to:
  - A topoisomerase I inhibitor payload, an exatecan derivative, via
  - A tetrapeptide-based cleavable linker
- HER3-DXd is in clinical evaluation for NSCLC, metastatic breast cancer, and colorectal cancer

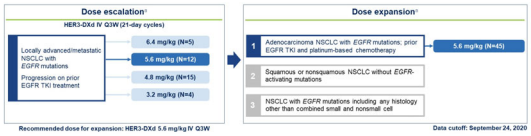
HER3 is expressed in 83% of NSCLC tumors[1,3]

HER3 alterations are not known to be a mechanism of resistance to EGFR TKI in *EGFR*m NSCLC



[1] HER3 overexpression is associated with metastatic progression and decreased relapse-free survival in patients with NSCLC.
1. Haratmoto Y, et al. *Clin Cancer Res*. 2019;25:7181-7191. 2. Nakada T, et al. *Chem Pharm Bull (Tokyo)*. 2019;67(3):173-185. 3. Ogitani Y, et al. *Clin Cancer Res*. 2016;22(20):5097-5108. 4. Kogamenaru S, et al. *Mol Cancer Ther*. 2019;18:2043-2050. 5. Haratani K, et al. *J Clin Invest*. 2020;130(1):374-388. 6. Ogitani Y, et al. *Cancer Sci*. 2016;107(7):1039-1046. 7. Scharpenseel H et al. *Sci Rep*. 2019;9(1):7406.

U31402-A-U102 is a Phase 1 Dose Escalation and Dose Expansion Study in Patients With NSCLC



57 patients with EGFR TKI–resistant, *EGFR*m NSCLC were treated with HER3-DXd 5.6 mg/kg in dose escalation (N=12) and dose expansion Cohort 1 (N=45)

- **Efficacy** evaluation in pooled patients with *EGFR*m NSCLC treated with HER3-DXd 5.6 mg/kg (**N=57**) (Median Follow Up: 10.2 mo; range, 5.2-19.9 mo)
- **Safety** evaluation in all patients in dose escalation and dose expansion Cohort 1 (**N=81**)

ClinicalTrials.gov, NCT03260491, EudraCT, 2017-000543-41, JapicCTI, 194888
[a] Patients with stable brain metastases were permitted to enroll. A prior biopsy was required prior to study entry but patients were not selected for inclusion based on measurement of HER3.

Patients with EGFRm NSCLC were Heavily Pre-treated with Majority Receiving Prior Platinum-based Chemotherapy

Patient Characteristics and Treatment History	HER3-DXd 5.6 mg/kg (N=57)	HER3-DXd All Doses (N=81)
Age, median (range), years	65 (40-80)	64 (40-80)
Female, n (%)	36 (63)	52 (64)
ECOG performance status 0/1, n (%)	23 (40) / 34 (60)	34 (42) / 47 (58)
Sum of diameters at baseline,[b] median (range), mm	54 (13-195)	51.5 (10-195)
History of CNS metastases, n (%)	27 (47)	43 (53)
Prior lines of systemic therapy, median (range)[c]	4 (1-9)	4 (1-9)
Prior cancer regimens		
Prior EGFR TKI therapy, n (%)	57 (100)	81 (100)
Prior osimertinib, n (%)	49 (86)	72 (89)
Prior platinum-based chemotherapy, n (%)	52 (91)	65 (80)
Prior immunotherapy, n (%)	23 (40)	28 (35)

Data cutoff: September 24, 2020
[b] By blinded independent central review per RECIST 1.1. [c] In the locally advanced or metastatic setting

HER3-DXd Demonstrated Durable Antitumor Activity After Failure of EGFR TKI and Platinum-based Chemotherapy (PBC)

Outcomes (BICR per RECIST 1.1) Median Follow Up: 10.2 (range, 5.2-19.9) mo[a]	HER3-DXd 5.6 mg/kg Prior TKI, ± PBC (N=57)	Prior OSI, PBC (N=44)
Confirmed ORR, % (95% CI)	39 (26-52)	39 (24-55)
Best overall response, n (%)		
CR	1 (2)	1 (2)
PR	21 (37)	16 (36)
SD, Non-CR/Non-PD	19 (33)	13 (30)
PD	9 (16)	8 (18)
Not evaluable	7 (12)	6 (14)
Disease control rate, % (95% CI)	72 (59-83)	68 (52-81)
Time to response, median (range), mo	2.6 (1.2-5.4)	2.7 (1.2-5.4)
Duration of response, median (95% CI), mo	6.9 (3.1-NE)	7.0 (3.1-NE)
PFS, median (95% CI), mo	8.2 (4.4-8.3)	8.2 (4.0-NE)

The subgroup of patients treated with prior **osimertinib (OSI)** and **platinum-based chemotherapy** demonstrated similar efficacy to the overall efficacy population

BICR, blinded independent central review; CR, complete response; NE, not evaluable; ORR, objective response rate; OSI, osimertinib; PBC, platinum-based chemotherapy; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease.
Data cutoff: September 24, 2020
[a] For patients treated with the recommended dose for expansion of HER3-DXd (N=57)

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6

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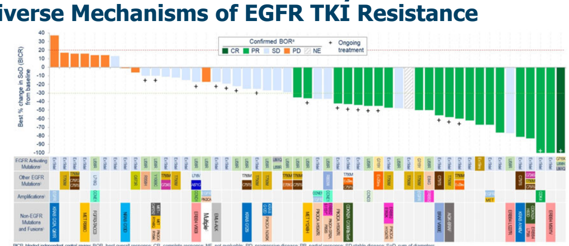
HER3-DXd Demonstrated Activity in Patients With Diverse Mechanisms of EGFR TKI Resistance



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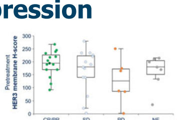
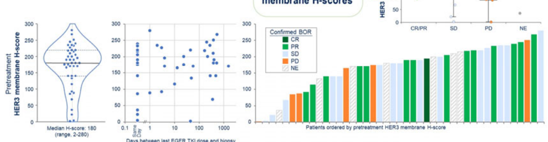
Clinical Responses Were Observed Across the Spectrum of Baseline HER3 Expression

- HER3 was expressed in all evaluable patients' (43/57) tumors
- HER3 expression was not correlated with time since last EGFR TKI dose

Responses were observed in patients with a wide range of baseline HER3 membrane H-scores





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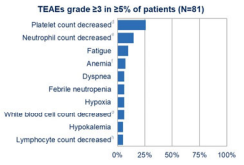
HER3-DXd Was Associated With a Manageable Safety Profile and a Low Rate of Discontinuations Due to Adverse Events

TEAEs, n (%) Median treatment duration: 5.7 (range, 0.7-28.3) mo	5.6 mg/kg (N=57)	All Doses (N=81)
Any TEAE	57(100)	81 (100)
Associated with treatment discontinuation[a]	6 (11)	7 (9)
Associated with treatment dose reduction	12 (21)	18 (22)
Associated with treatment dose interruption	21 (37)	30 (37)
Associated with death[b]	4 (7)	5 (6)
Grade ≥3 TEAE	42 (74)	52 (64)
Treatment-related TEAE:	55 (96)	78 (96)
Associated with death	0	0
Grade ≥3	31 (54)	38 (47)
Serious TEAE	12 (21)	15 (19)
Interstitial lung disease[c]	4 (7)	4 (5)
Grade 1	2 (4)	2 (2)
Grade 2	1 (2)	1 (1)
Grade 3	1 (2)	1 (1)
Grade 4/5	0	0



- The rate of adjudicated treatment-related interstitial lung disease was 5%; none were grade 4/5
- Median time to adjudicated onset of treatment-related interstitial lung disease was 53 (range, 13-130) days

Data cutoff: September 24, 2020.
[a] TEAEs associated with treatment discontinuation were fatigue (2), nausea, decreased appetite, interstitial lung disease, neutrophil count decreased, pneumonitis, and upper respiratory tract infection; none were for thrombocytopenia (1 each). [b] TEAEs associated with death were: disease progression (2), respiratory failure (2), and shock (1). [c] One additional occurrence of Grade 5 ILD was determined by adjudication to be unrelated to study treatment. [1] Includes thrombocytopenia. [2] Includes neutropenia. [3] Includes hemoglobin decreased. [4] Includes leukopenia. [5] Includes lymphopenia.

HER3-DXd: Targeting the unmet medical need in EGFR-TKI resistant EGFRm NSCLC

Antitumor activity

Clinically meaningful, durable efficacy (ORR, 39%; median PFS, 8.2 months)
- Efficacy shown across EGFR TKI resistance mechanisms in a difficult to treat patient population
- Antitumor activity observed across a wide range of baseline HER3 expression

Safety

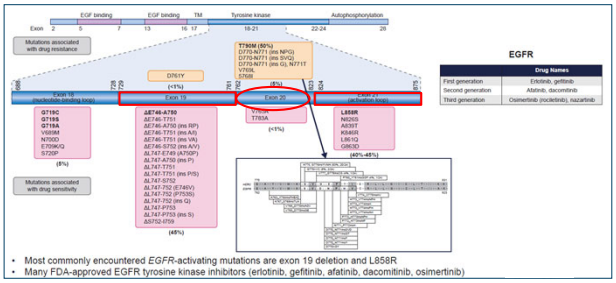
Tolerable and manageable safety profile
- Low rate of discontinuation due to AEs (7/81; none due to thrombocytopenia)
- Low rate of treatment-related interstitial lung disease (4/81; none were grade 4/5)

Ongoing development in *EGFR*m NSCLC

Study/Phase	Patients	Treatment	NCT
Ph1 (current study)	Post-TKI, Post-PBC	HER3-DXd	NCT03260491
Ph2 pivotal study	Post-TKI, Post-PBC	HER3-DXd	NCT04619004
Ph1 study	Post-OSI, Pre-PBC	HER3-DXd + OSI	NCT04676477

EXON 20

Complexity of EGFR Alterations in Lung Cancer

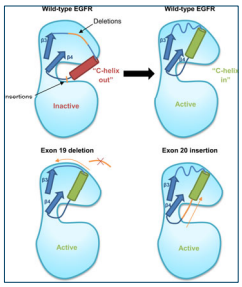


- Most commonly encountered *EGFR*-activating mutations are exon 19 deletion and L858R
- Many FDA-approved EGFR tyrosine kinase inhibitors (erlotinib, gefitinib, afatinib, dacomitinib, osimertinib)

Nature Reviews Cancer 2007. Epidermal growth factor receptor mutations in lung cancer
S. Sharma, D. Bell, J. Settleman, D. Haber

GW ONCOLOGY UPDATE 28

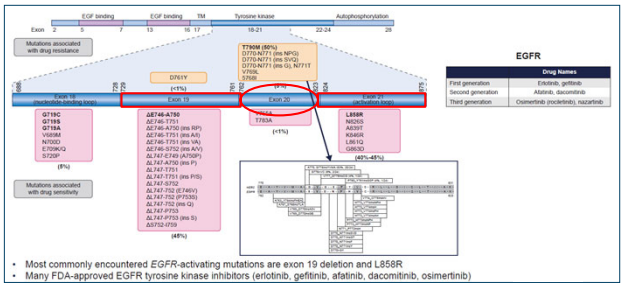
EGFR exon 20



- Mutations in exon 20 lead to different structural arrangement for C-helix protein vs exon 19 and 21
- This creates a narrower therapeutic window that cannot be targeted or drugged by first generation TKIs
- Different therapies are thus needed to inhibit exon 20 kinase activity

GW ONCOLOGY UPDATE 29

Complexity of *EGFR* Alterations in Lung Cancer



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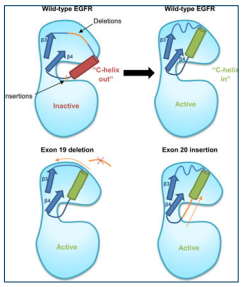
Nature Reviews Cancer 2007. Epidermal growth factor receptor mutations in lung cancer
S. Sharma, D. Bell, J. Settleman, D. Haber

GW ONCOLOGY UPDATE 30

EGFR exon 20



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- This creates a narrower therapeutic window that cannot be targeted or drugged by first generation TKIs
- Different therapies are thus needed to inhibit exon 20 kinase activity

Targeting EGFR Exon 20 Insertions in Lung Cancer

***EGFR* exon 20 insertions comprise 4%-10% of *EGFR*-mutant NSCLC and are generally refractory to first/second-generation EGFR TKIs, but other agents are showing clinical activity and tolerability in this setting**

- **Osimertinib**
  - Phase 2 EA5162 trial (NCT03191149)[1]
- **Poziotinib**
  - Phase 2 trial (NCT03066206)[2]
  - Phase 2 ZENITH20 trial did not meet primary endpoint in *EGFR* exon 20 cohort[3]
- **Mobocertinib (TAK-788)**
  - Phase 1/2 trial "EXCLAIM" extension cohort (NCT02716116)[4]
- Breakthrough therapy designation based on ORR and long-term benefit seen in a phase 1/2 study in patients with exon20ins disease[5]
- **Amivantamab (JNJ-61186372)**
  - Phase 1 study (NCT02609776) demonstrated robust and durable antitumor activity in patients with exon20ins disease with a manageable safety profile[6]
  - **FDA approved 5/21/21 for EXON 20 after platinum chemo

1. Piotrowska Z et al. ASCO 2020. Abstract 9513. 2. Robichaux JP et al. Nat Med. 2018;24:638-646. 3. Le X et al. ASCO 2020. Abstract 9514. 4. Riely G et al. WCLC 2019. P1.01-127. 5. Janne PA et al. J Clin Oncol. 2019;37(suppl 15):9007. 6. Park K et al. ASCO 2020. Abstract 9512.

Amivantamab in Post-platinum EGFR Exon 20 Insertion Mutant Non-small Cell Lung Cancer

Joshua K. Sabari[1], Catherine A. Shu[2], Keunchil Park[3], Natasha B. Leighl[4], Paul Mitchell[5], Sang-We Kim[6], Jong-Seok Lee[7], Dong-Wan Kim[8], Santiago Viteri[9], Alexander I. Spira[10], Ji-Youn Han[11], José Trigo[12], Chee Khoon Lee[13], Ki Hyeong Lee[14], Nicolas Girard[15], Tsung-Ying Yang[16], Koichi Goto[17], Rachel E. Sanborn[18], James Chih-Hsin Yang[19], Joshua C. Curtin[20], John Xie[20], Amy Roshak[20], Meena Thayu[20], Roland E. Knoblauch[20], Byoung Chul Cho[21]

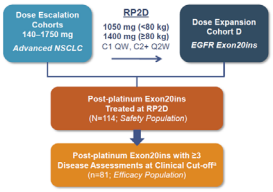
[1]New York University School of Medicine, New York, NY, USA, [2]Columbia University Medical Center, New York, USA, [3]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea, [4]Princess Margaret Cancer Centre, Toronto, Canada, [5]Olivia Newton-John Cancer Wellness and Research Centre, Austin Hospital, Heidelberg, Australia, [6]Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea, [7]Seoul National University Bundang Hospital, Seongnam, Republic of Korea, [8]Seoul National University Hospital, Seoul, Republic of Korea, [9]Instituto Oncológico Dr. Rosell, Hospital Universitari Dexeus, Grupo QuirónSalud, Barcelona, Spain, [10]Virginia Cancer Specialists Research Institute, USOncology Research, Fairfax, VA, USA, [11]National Cancer Center, Gyeonggi-do, Republic of Korea, [12]Hospital Universitario Virgen de la Victoria y Regional, IBIMA, Málaga, Spain, [13]St George Hospital, Kogarah, Australia, [14]Chungbuk National University Hospital, Cheongju, Republic of Korea, [15]Institut Curie, Paris, France, [16]Taichung Veterans General Hospital, Taiwan, Republic of China, [17]National Cancer Center Hospital East, Kashiwa, Japan, [18]Earle A. Chiles Research Institute, Providence Cancer Institute, Portland, OR, USA, [19]National Taiwan University Cancer Center, Taiwan, Republic of China, [20]Janssen R&D, Spring House, PA, USA, [21]Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Republic of Korea

CHRYSALIS Study Design: Post-platinum Exon20ins Population

NCT02609776

Key Objectives
- Dose escalation: Establish RP2D
- Dose expansion: Assess safety and efficacy at RP2D

Key Eligibility Criteria for Post-platinum Population
- Metastatic/unresectable NSCLC
- EGFR Exon20ins mutation
- Progressed on platinum-based chemotherapy



Efficacy End Points

Primary
- Overall response rate per RECIST v1.1

Key Secondary
- Clinical benefit rate
- Duration of response
- Progression-free survival
- Overall survival

[a]Post-platinum patients treated at the RP2D and had ≥3 scheduled disease assessments or discontinued, progressed, or died prior to the 3rd postbaseline assessment at the time of clinical cut-off (June 8, 2020). By October 8, 2020, all responders in the efficacy population had ≥6 months of follow-up from their first disease assessment.
C, cycle; Q2W, every other week; QW, weekly; RECIST, Response Evaluation Criteria in Solid Tumors; RP2D, recommended phase 2 dose

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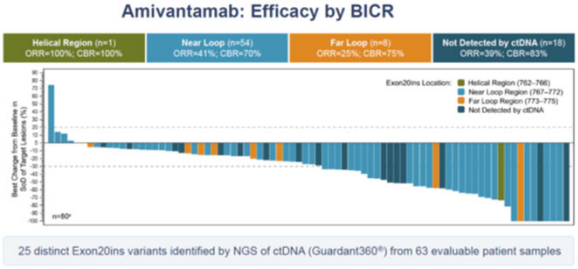
Amivantamab: Efficacy by BICR



25 distinct Exon20ins variants identified by NGS of ctDNA (Guardant360®) from 63 evaluable patient samples

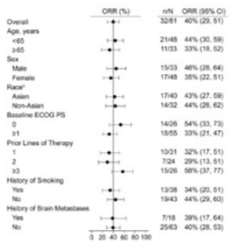
Sabari JK, Shu CA, Park K, et al. Presented at: IASLC 2020 World Conference on Lung Cancer Singapore. January 28-31, 2021. Abstract OA04.04

GW ONCOLOGY UPDATE 35

Amivantamab: Efficacy by BICR

BICR-assessed Response	Efficacy Population (n=81)
Overall response rate	**40%** (95% CI, 29–51)
Median duration of response	**11.1 months** (95% CI, 6.9–NR)
Best response, n (%)	
Complete response	3 (4)
Partial response	29 (36)
Stable disease	39 (48)
Progressive disease	8 (10)
Not evaluable	1 (1)
Clinical benefit rate[a]	74% (95% CI, 63–83)

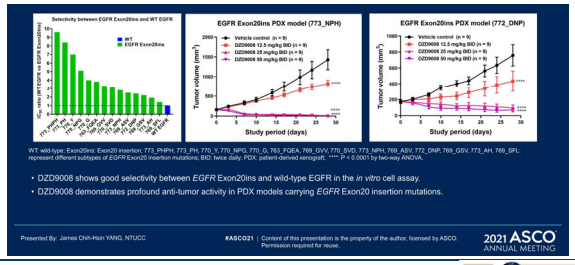
Median follow-up: 9.7 months (range, 1.1–29.3)



Sabari JK, Shu CA, Park K, et al. Presented at: IASLC 2020 World Conference on Lung Cancer Singapore. January 28-31, 2021. Abstract OA04.04

GW ONCOLOGY UPDATE 36

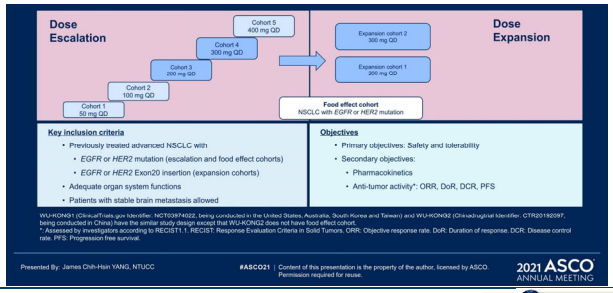
DZD9008 Is A Potent and Selective EGFR Exon20 Insertion Inhibitor



WT: wild-type; Exon20ins: Exon20 insertion; 773_PHPH: 773_PH_T 770_NPG; 770_G 763_FQEA 769_GVV; 770_SVD; 773_NPH; 769_ASV; 772_DNP; 769_GSV; 773_AH; 769_SFL: represent different subtypes of EGFR Exon20 insertion mutations; BID: twice daily; PDX: patient-derived xenograft; ****: P < 0.0001 by two-way ANOVA.

- DZD9008 shows good selectivity between *EGFR* Exon20ins and wild-type EGFR in the *in vitro* cell assay.
- DZD9008 demonstrates profound anti-tumor activity in PDX models carrying *EGFR* Exon20 insertion mutations.

Phase 1 Study Design Overview



WU-KONG1 (ClinicalTrials.gov Identifier: NCT03974022, being conducted in the United States, Australia, South Korea and Taiwan) and WU-KONG2 (ChinaDrugtrial Identifier: CTR20192097, being conducted in China) have the similar study design except that WU-KONG2 does not have food effect cohort.
*: Assessed by investigators according to RECIST1.1. RECIST: Response Evaluation Criteria in Solid Tumors, ORR: Objective response rate, DoR: Duration of response, DCR: Disease control rate, PFS: Progression free survival.

Demographic and Baseline Characteristics of Patients Treated with DZD9008

Characteristics	Safety set (N = 102)	Efficacy set (N = 56)
Median age, y (range)	59 (32 - 85)	59 (32 - 85)
Female, n (%)	57 (56)	33 (58.9)
Race (White/Asian), n (%),	17 (16.7)/85 (83.3)	8 (14.3)/48 (85.7)
ECOG (0/>1), n (%)	38 (37.3)/64 (62.7)	18 (32.1)/38 (67.9)
Prior systemic anti-cancer treatment		
Lines, Median (range)	3 (1-10)	2 (1-10)
Chemotherapy, n (%)	93 (91.2)	52 (92.9)
EGFR TKIs, n (%)	47 (46.1)	25 (44.6)
Poziotinib	3 (2.9)	2 (3.6)
TAK-788	1 (1.0)	0 (0.0)
Immunotherapy, n (%)	35 (34.3)	17 (30.4)
Amivantamab, n (%)	5 (4.9)	4 (7.1)
Others, n (%)	25 (24.5)	11 (19.6)
Baseline brain metastasis, n (%)	44 (43.1)	23 (41.1)
Prior brain radiotherapy	27 (61.4)	14 (60.9)

*ECOG: Eastern Cooperative Oncology Group

Common Drug-Related AEs

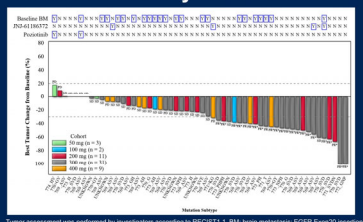
Drug related adverse event by preferred term (n, %)	n = 102	
	All grade	CTCAE grade ≥ 3
Diarrhea	55 (53.9)	5 (4.9)
Rash	41 (40.2)	0 (0.0)
Nausea	35 (34.3)	0 (0.0)
Anemia	29 (28.4)	4 (3.9)
Paronychia	28 (27.5)	2 (2.0)
Decreased appetite	27 (26.5)	2 (2.0)
Vomiting	26 (25.5)	1 (1.0)
Blood creatinine phosphokinase increased	23 (22.5)	7 (6.9)
Mouth ulceration	15 (14.7)	0 (0.0)
Blood creatinine increased	15 (14.7)	0 (0.0)
Amylase increased	14 (13.7)	1 (1.0)
Lipase increased	14 (13.7)	2 (2.0)
Aspartate aminotransferase increased	13 (12.7)	2 (2.0)

* Only AEs with frequency > 10% were listed.
- AEs were assessed as drug-related by investigators.
- Data were summarized across all dose levels from 50 mg to 400 mg.
- Drug-related AEs were consistent with other EGFR TKIs, mainly diarrhea and skin rash. Majorities of the AEs were grade 1 or 2.

Presented By: James Chih-Hsin YANG, NTUCC

40

Antitumor Activity of DZD9008 in *EGFR* Exon20 Insertion



Mutation subtypes	ORR[a] n (%)	DCR n (%)
V769_D770insASV (N = 20)	8 (40.0)	19 (90.0)
D770_N771insSVD (N = 10)	6 (60.0)	9 (90.0)
Other subtypes* (N = 18)	7 (38.9)	15 (83.3)
Unknown subtypes (N = 5)	0 (0.0)	4 (80.0)
All (N = 53)	21 (39.6)	46 (86.8)

Data was analyzed at dose levels with observed response (≥ 100 mg);
[a]: Confirmed ORR
*: Other subtypes of *EGFR* Exon20 insertion include: V774_C775insHV, D770delinsDV, V769_D770insASV, H773_V774insH, H773_V774insAH, D770_N771insG, H773_V774insPHPH and N771_P772insSVDN

Tumor assessment was performed by investigators according to RECIST1.1. BM: brain metastasis; EGFR Exon20 insertion subtypes were confirmed by next-generation sequencing (NGS) using tumor tissue or/and plasma ctDNA.

- Antitumor efficacy observed at the doses ≥ 100 mg, and across different EGFR Exon20 insertion subtypes
- Tumor response observed in patients with brain metastasis
- Tumor response observed in patients with prior JNJ-61186372 (Amivantamab) treatment

Presented By: James Chih-Hsin YANG, NTUCC

Antitumor Activity of DZD9008 in EGFR Exon20 Insertion

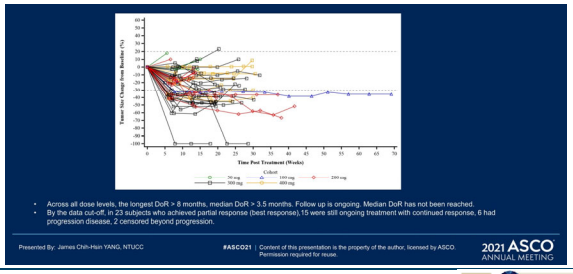
	50 mg QD (N = 3)	100 mg QD (N = 2)	200 mg QD (N = 11)	300 mg QD (N = 31)	400 mg QD (N = 9)	All (N = 56)
Best response, n (%)						
Partial response (unconfirmed)	0 (0.0)	1 (50.0)	5 (45.5)	15 (48.4)	2 (22.2)	23 (41.1)
Partial response (confirmed)	0 (0.0)	1 (50.0)	5 (45.5)	13 (41.9)	2 (22.2)	21 (37.5)
Stable disease	2 (66.7)	1 (50.0)	4 (36.4)	15 (48.4)	5 (55.6)	27 (48.2)
Progressive disease	1 (33.3)	0 (0.0)	2 (18.2)	3 (9.7)	2 (22.2)	8 (14.3)
Confirmed ORR, n (%)	0 (0.0)	1 (50.0)	5 (45.5)	13 (41.9)	2 (22.2)	21 (37.5)
DCR, n (%)	2 (66.7)	2 (100.0)	9 (81.8)	28 (90.3)	7 (77.8)	48 (85.7)

Tumor assessment was performed by investigators according to RECIST1.1; QD: once daily

Presented By: James Chih-Hsin YANG, NTUCC

42

Durable Antitumor Activity in Patients with *EGFR* Exon20 Insertion



- Across all dose levels, the longest DoR > 8 months, median DoR > 3.5 months. Follow up is ongoing. Median DoR has not been reached.
- By the data cut-off, in 23 subjects who achieved partial response (best response),15 were still ongoing treatment with continued response, 6 had progression disease, 2 censored beyond progression.

Presented By: James Chih-Hsin YANG, NTUCC

43

KRAS G12C

44

Phase 2 CodeBreaK100 Trial Design

Screening / Enrolment

Key Eligibility:

- Locally advanced or metastatic NSCLC
- *KRAS* p.G12C mutation as assessed by central testing of tumor biopsies
- Progressed on prior standard therapies[a]
- Stable brain metastases were allowed

ClinicalTrials.gov identifier: NCT03600883

Sotorasib was orally administered at 960 mg once daily until disease progression[b]

Radiographic scan every 6 weeks up to week 48 and once every 12 weeks thereafter

Primary endpoint: ORR (RECIST 1.1) by independent central review
Key secondary endpoints: DoR; disease control rate; TTR; PFS; OS; safety
Exploratory endpoints: Evaluation of biomarkers

Safety and Long-term Follow-up[c]

a: no more than 3 prior lines of therapies were allowed; b: treatment beyond disease progression was allowed if certain criteria were met; c: safety follow-up occurs 30 (+7) days after the last dose of sotorasib; long-term follow-up occurs every 12 (±2) weeks for up to 3 years. NSCLC: non-small cell lung cancer; ORR: objective response rate; DoR: duration of response; TTR: time to response; PFS: progression-free survival; OS: overall survival; RECIST: Response Evaluation Criteria in Solid Tumors.

Presented By: **Ferdinandos Skoulidis, M.D., Ph.D.**
Data cutoff: March 15, 2021; Median follow-up time: 15.3 months

45

Baseline Characteristics

Baseline Characteristics	Sotorasib 960mg, QD N = 126
Median age – years (range)	63.5 (37–80)
ECOG performance status – n (%)	
0	38 (30.2)
1	88 (69.8)
Smoking history – n (%)	
Never	6 (4.8)
Current or former	117 (92.9)
Prior lines of systemic anticancer therapy – n (%)	
1	54 (42.9)
2	44 (34.9)
3	28 (22.2)
Types of prior anticancer therapy – n (%)	
Platinum-based chemotherapy	113 (89.7)
PD-1 or PD-L1 inhibitors	115 (91.3)
Platinum-based chemotherapy and PD-1/PD-L1 inhibitors	102 (81.0)

ECOG: Eastern Cooperative Oncology Group; QD: once a day; PD-1: programmed cell death protein 1; PD-L1: programmed death-ligand 1.

Most patients were previously treated with both platinum-based chemotherapy and immunotherapy

46

Tumor Response

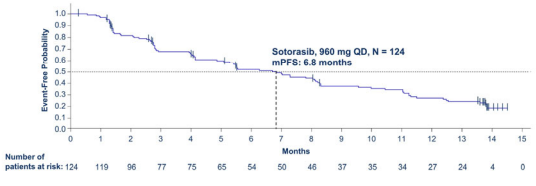
	Sotorasib 960mg, QD N = 124[a]
Objective Response Rate – % (95% CI)	37.1 (28.6, 46.2)
Best Overall Response – n (%)	
Complete response	4 (3.2)
Partial response	42 (33.9)
Stable disease	54 (43.5)
Progressive disease	20 (16.1)
Not evaluable or missing scan[b]	4 (3.2)
Disease Control Rate – % (95% CI)	80.6 (72.6, 87.2)
Duration of Response – months	
Median (95% CI)	11.1 (6.9, NE)
Time to Response – months	
Median (min, max)	1.35 (1.2, 10.1)

a: according to central review, 2 patients did not have measurable lesions at baseline per RECIST 1.1 and were excluded from response assessment; b: 2 patients stopped treatment without postbaseline scans and were deemed as "missing scan"; 2 patients had 1 postbaseline scan and were assessed as "not evaluable" by central review.
CI: confidence interval; NE: not evaluable; QD: once a day; RECIST: Response Evaluation Criteria in Solid Tumors.

Over 80% of patients achieved disease control with sotorasib, including 4 complete responses and 42 partial responses

47

Progression-Free Survival

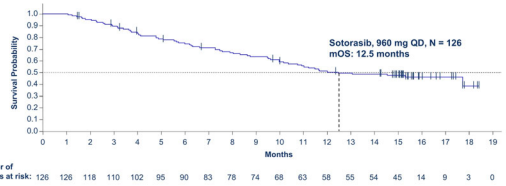


QD: once a day; mPFS: median progression-free survival; CI: confidence interval.

Median progression-free survival was 6.8 months (95% CI: 5.1, 8.2)

48

Overall Survival



QD: once a day; mOS: median overall survival; CI: confidence interval.

Median overall survival was 12.5 months (95% CI: 10.0, not evaluable)

Presented By: **Ferdinandos Skoulidis, M.D., Ph.D.**
Data cutoff: March 15, 2021; Median follow-up time: 15.3 months

2021 ASCO ANNUAL MEETING

GW ONCOLOGY UPDATE 49

Safety

Treatment-Related Adverse Events (TRAEs) Occurring in > 5%	Any Grade N = 126 n (%)	Grade 3 N = 126 n (%)
Any TRAEs	88 (69.8)	25 (19.8)
Diarrhea	40 (31.7)	5 (4.0)
Nausea	24 (19.0)	0
ALT increase	19 (15.1)	8 (6.3)
AST increase	19 (15.1)	7 (5.6)
Fatigue	14 (11.1)	0
Vomiting	10 (7.9)	0
Blood alkaline phosphatase increase	9 (7.1)	1 (0.8)
Maculopapular rash	7 (5.6)	0

One patient (0.8%) reported grade 4 TRAEs (pneumonitis and dyspnea)

- **No fatal TRAEs occurred**
- **TRAEs led to dose modifications in 28 patients (22.2%)**
- **TRAEs led to treatment discontinuation in 9 patients (7.1%)**
  - Drug-induced liver injury (n=3, 2.4%)
  - LFT increase (n=1, 0.8%)
  - ALT increase (n= 2, 1.6%)
  - AST increase (n=2, 1.6%)
  - Blood alkaline phosphatase increase (n=1, 0.8%)
  - Transaminases increase (n=1, 0.8%)
  - Pneumonitis (n=2, 1.6%)
  - Dyspnea (n=1, 0.8%)

ALT: alanine aminotransferase; AST: aspartate aminotransferase; LFT: liver function test.

Treatment-related adverse events were mostly grade 1 or 2 and were generally manageable

Presented By: **Ferdinandos Skoulidis, M.D., Ph.D.**
Data cutoff: March 15, 2021; Median follow-up time: 15.3 months

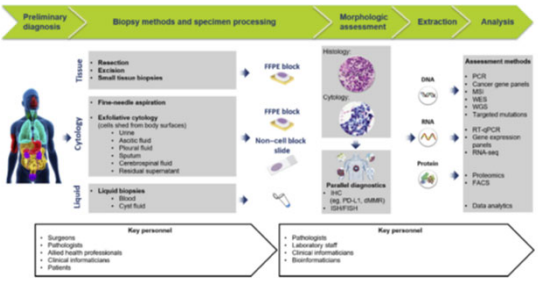
2021 ASCO ANNUAL MEETING

GW ONCOLOGY UPDATE 50

TESTING

GW ONCOLOGY UPDATE 51

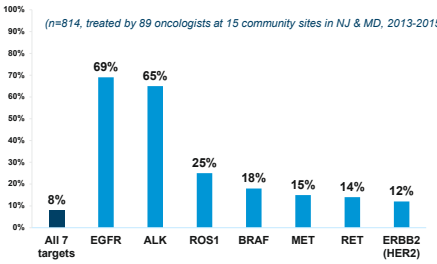
Tissue Journey



GW ONCOLOGY UPDATE 52

Genotyping Rates for NCCN Genomic Targets in Non-Small Cell Lung Cancer (Stage IIIB/IV, Non-Squamous)

(n=814, treated by 89 oncologists at 15 community sites in NJ & MD, 2013-2015)



Gutierrez et al. 2017 *Clinical Lung Cancer*

GW ONCOLOGY UPDATE 53

2021 ASCO ANNUAL MEETING

BIOMARKER TISSUE JOURNEY AMONG PATIENTS WITH UNTREATED METASTATIC NON-SMALL CELL LUNG CANCER IN THE US ONCOLOGY NETWORK COMMUNITY PRACTICES

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June 4-8, 2021

GW ONCOLOGY UPDATE 54

Methods

- Retrospective, observational chart review
- Patients with mNSCLC initiating first-line (1L) systemic therapy between April 1, 2018 and March 31, 2020
- Data from practices within The US Oncology Network of community oncology practices that utilize a similar electronic health record

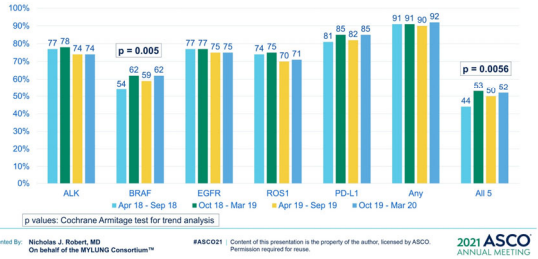
55

Patient Characteristics

	Overall N=3474	Nonsquamous N=2820
Age at mNSCLC, years		
Median(Min, Max)	69 (23,90+)	69 (24,90+)
Gender, %		
Female	51.1	53.9
Male	48.9	46.1
Race, %		
White	65.3	64.4
Black Or African American	8.3	8.3
Other	5.8	6.0
Not documented	20.7	21.2
Practice region, %		
South	46.4	45.5
West	35.3	36.2
Midwest	11.6	12.1
Northeast	6.6	6.3

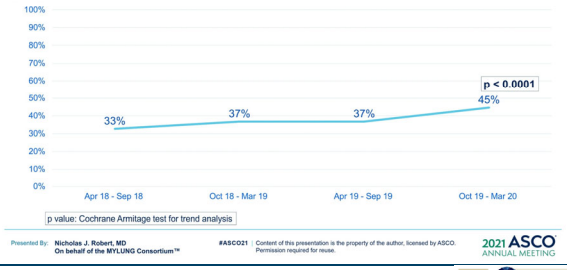
56

Biomarker testing rates over time for overall study population



57

NGS testing rates over time for the overall population



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58

ADJUVANT TRIALS

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59

IMpower010: study design

Completely resected stage IB-IIIA NSCLC per UICC/AJCC v7
- Stage IB tumors ≥4 cm
- ECOG 0-1
- Lobectomy/pneumonectomy
- Tumor tissue for PD-L1 analysis

Cisplatin + pemetrexed, gemcitabine, docetaxel or vinorelbine
1-4 cycles
N=1280

R 1:1

No crossover

Atezolizumab 1200 mg q21d 16 cycles
N=1005

BSC

Survival follow-up

Stratification factors
- Male/female
- Stage (IB vs II vs IIIA)
- Histology
- PD-L1 tumor expression status[a]: TC2/3 and any IC vs TC0/1 and IC2/3 vs TC0/1 and IC0/1

Primary endpoints
- Investigator-assessed DFS tested hierarchically:
  - PD-L1 TC ≥1% (per SP263) stage II-IIIA population
  - All-randomized stage II-IIIA population
  - ITT population (stage IB-IIIA)

Key secondary endpoints
- OS in ITT population
- DFS in PD-L1 TC ≥50% (per SP263) stage II-IIIA population
- 3-y and 5-y DFS in all 3 populations

Both arms included observation and regular scans for disease recurrence on the same schedule.
ECOG, Eastern Cooperative Oncology Group; IC, tumor-infiltrating immune cells; ITT, intent to treat; TC, tumor cells. [a]Per SP142 assay.

3

Presented By: Dr. Heather A. Wakelee IMpower010 Interim Analysis https://bit.ly/3316JJP

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60

IMpower010: statistical analysis plan

DFS in PD-L1 TC ≥1% stage II–IIIA population
2-sided α=0.05

If positive:

DFS in all-randomized stage II–IIIA population
2-sided α=0.05

If positive:

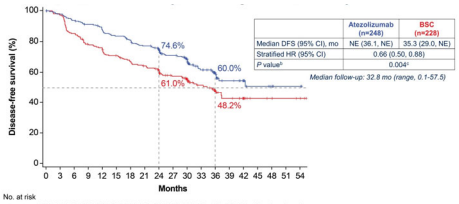
DFS in ITT population (stage IB-IIIA)
2-sided α=0.05

If positive:

OS in ITT population
2-sided α=0.05

- The primary DFS endpoint was tested hierarchically in 3 primary analysis populations

IMpower010: DFS in the PD-L1 TC ≥1%[a] stage II-IIIA population (primary endpoint)

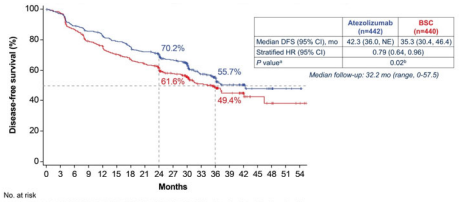


	Atezolizumab (n=248)	BSC (n=228)
Median DFS (95% CI), mo	NE (36.1, NE)	35.3 (29.0, NE)
Stratified HR (95% CI)	0.66 (0.50, 0.88)	
P value[a]	0.004[c]	

Median follow-up: 32.8 mo (range, 0.1-57.5)

Clinical cutoff: January 21, 2021. CI, confidence interval; HR, hazard ratio; NE, not evaluable. [a] Per SP263 assay. [b] Stratified log-rank. [c] Crossed the significance boundary for DFS.

IMpower010: DFS in the all-randomized stage II-IIIA population (primary endpoint)

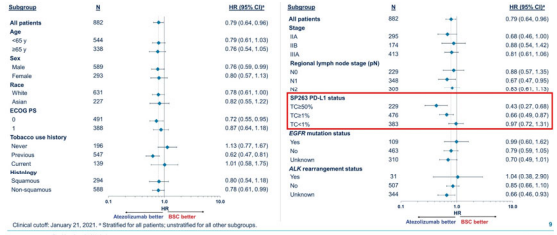


	Atezolizumab (n=442)	BSC (n=440)
Median DFS (95% CI), mo	42.3 (36.0, NE)	35.3 (30.4, 46.4)
Stratified HR (95% CI)	0.79 (0.64, 0.96)	
P value[a]	0.02[b]	

Median follow-up: 32.2 mo (range, 0-57.5)

Clinical cutoff: January 21, 2021. [a] Stratified log-rank. [b] Crossed the significance boundary for DFS.

IMpower010: DFS in key subgroups of the all-randomized stage II-IIIA population



Clinical cutoff: January 21, 2021. a Stratified for all patients; unstratified for all other subgroups.

9

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IMpower010 Interim Analysis
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64

IMpower010: statistical analysis plan

DFS in PD-L1 TC ≥1% stage II–IIIA population
2-sided α=0.05

If positive:

DFS in all-randomized stage II–IIIA population
2-sided α=0.05

If positive:

DFS in ITT population (stage IB-IIIA)
2-sided α=0.05

If positive:

OS in ITT population
2-sided α=0.05

- The significance boundary was not crossed at this DFS interim analysis in the ITT population (stage IB-IIIA) and testing will continue to the final DFS analysis in this population

10

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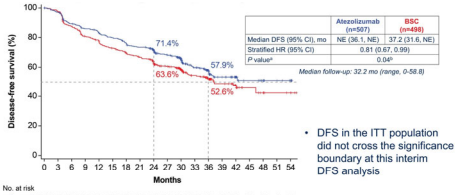
IMpower010: DFS in the ITT population (stage IB-IIIA; primary endpoint



	Atezolizumab (n=507)	BSC (n=488)
Median DFS (95% CI), mo	NE (36.1, NE)	37.2 (31.6, NE)
Stratified HR (95% CI)	0.81 (0.67, 0.99)	
P value[b]	0.04[b]	

Median follow-up: 32.2 mo (range, 0-58.8)

- DFS in the ITT population did not cross the significance boundary at this interim DFS analysis

Clinical cutoff: January 21, 2021. a Stratified log-rank. b The statistical significance boundary for DFS was not crossed.

11

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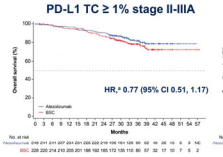
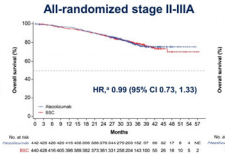
IMpower010: early OS data at interim DFS analysis

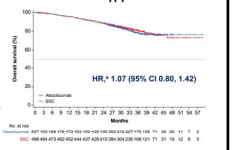
PD-L1 TC ≥ 1% stage II-IIIA



All-randomized stage II-IIIA



ITT



- OS data were immature at this pre-planned DFS interim analysis
  - OS in the ITT population was not formally tested
  - A trend toward OS improvement with atezolizumab was seen in the PD-L1 TC ≥1% stage II-IIIA population

Clinical cutoff: January 21, 2021. ªStratified.

12

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67

AACR American Association for Cancer Research

Nivolumab + platinum-doublet chemotherapy vs chemotherapy as neoadjuvant treatment for resectable (IB–IIIA) non-small cell lung cancer in the phase 3 CheckMate 816 trial

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Presentation Number CT003

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68

CheckMate 816 study designa

Key Eligibility Criteria

- Newly diagnosed, resectable, stage IB (≥ 4 cm)–IIIA NSCLC (per TNM 7th edition)
- ECOG performance status 0–1
- No known sensitizing *EGFR* mutations or *ALK* alterations

Stratified by Stage (IB–II vs IIIA), PD-L1[b] (≥ 1% vs < 1%[c]), and sex

N = 358

R 1:1

- NIVO 360 mg Q3W + chemo[d] Q3W (3 cycles)
- Chemo[d] Q3W (3 cycles)
- NIVO 3 mg/kg Q2W (3 cycles) + IPI 1 mg/kg (cycle 1 only)[f]

Radiologic restaging → Surgery (within 6 weeks post-treatment) → Optional adjuvant chemo ± RT[g] → Follow-up

Database lock: September 16, 2020; minimum follow-up: 7.6 months for NIVO + chemo and chemo arms.

[a]NCT02998528; [b]Determined by the PD-L1 IHC 28-8 pharmDx assay (Dako); [c]Included patients with PD-L1 expression status not evaluable and indeterminate; [d]NSQ: pemetrexed + cisplatin or paclitaxel + carboplatin; SQ: gemcitabine + cisplatin or paclitaxel + carboplatin; [e]Vinorelbine + cisplatin, docetaxel + cisplatin, gemcitabine + cisplatin (SQ only), pemetrexed + cisplatin (NSQ only), or paclitaxel + carboplatin; [f]Randomized exploratory arm (enrollment closed early); [g]Per healthcare professional choice.

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69

Methods

Pathological assessment (primary and secondary endpoints)

- Performed via a blinded independent pathological review (BIPR) committee based on immune-related pathological response criteria described previously[1]
  - pCR: 0% residual viable tumor cells in **both** primary tumor (lung) and sampled lymph nodes[a]
  - MPR: ≤10% residual viable tumor cells in **both** primary tumor (lung) and sampled lymph nodesa

a Lymph nodes from at least 5 stations were recommended to be sampled.
1. Cottrell TR, et al. Ann Oncol 2018:29:1853–1860.

GW ONCOLOGY UPDATE 70

Baseline characteristics

	NIVO + chemo (n = 179)	Chemo (n = 179)
Age, median (range), years	64 (41–82)	65 (34–84)
Female, %	28	29
Region,[a] %		
North America	23	28
Europe	23	14
Asia	48	51
Stage,[b] %		
IB–II[c]	36	35
IIIA	63	64
Histology, %		
Squamous	49	53
Non-squamous	51	47
Smoking status,[d] %		
Current / former	89	88
Never	11	11

	NIVO + chemo (n = 179)	Chemo (n = 179)
Tumor PD-L1 expression, %[e]		
Not evaluable	7	7
< 1%	44	43
≥ 1%	50	50
1–49%	28	26
≥ 50%	21	24
TMB, %[e]		
Not evaluable / not reported[f]	51	50
< 12.3 mut/Mb	27	30
≥ 12.3 mut/Mb	22	21

- Baseline characteristics in the NIVO + IPI (exploratory) arm were generally similar to the NIVO + chemo and chemo arms

[a]Rest of the world: 7% of patients in each of the NIVO + chemo and chemo arms; [b]Disease stage by CRF, with TNM 7th edition used for classification; 1 patient in each of the NIVO + chemo and chemo arms had stage IV disease; [c]Stage IB, IIA, IIB disease: 6%, 17%, and 14% of patients in the NIVO + chemo arm, and 4%, 18%, and 13% in the chemo arm, respectively; [d]Smoking status unknown: 1 patient in chemo arm; [e]Percentages are based on ITT; [f]TMB was not analyzed for patients in China, and these patients are included in the "not reported" category.

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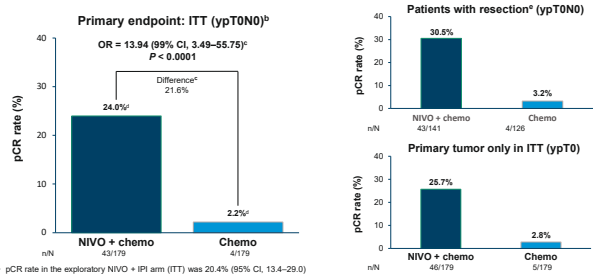
Primary endpoint: pCRa rate with neoadjuvant NIVO + chemo vs chemo



- pCR rate in the exploratory NIVO + IPI arm (ITT) was 20.4% (95% CI, 13.4–29.0)

[a]For BIPR: pCR: 0% residual viable tumor cells in both primary tumor (lung) and sampled lymph nodes; [b]ITT principle: patients who did not undergo surgery counted as non-responders for primary analysis; [c]Calculated by stratified Cochran-Mantel-Haenszel method; [d]pCR rates 95% CI: NIVO + chemo, 18.0-31.0; chemo, 0.6-5.6; [e]Patients who underwent definitive surgery with an evaluable pathology sample for BIPR.

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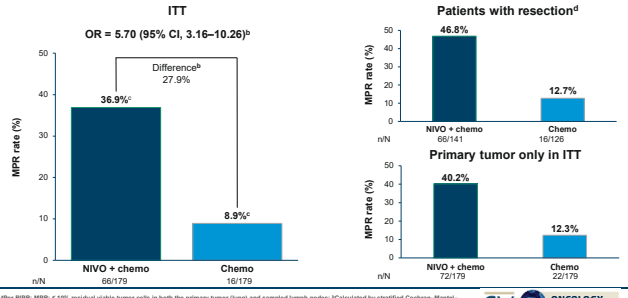
MPRa rate with neoadjuvant NIVO + chemo vs chemo



[a]Per BIPR; MPR: ≤ 10% residual viable tumor cells in both the primary tumor (lung) and sampled lymph nodes; [b]Calculated by stratified Cochran–Mantel–Haenszel method; [c]MPR rates 95% CI: NIVO + chemo, 29.8-44.4; chemo, 5.2-14.1; [d]Patients who underwent definitive surgery with an evaluable pathology sample for BIPR.

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Summary

- Genotyping is critical
  - Consider both tissue and plasma
- The list of genotypes that is actionable is growing
  - EGFR EXON 20
  - KRAS G12C
  - HER2?
- Neoadjuvant/Adjuvant immunotherapy will most likely improve the outcomes for patients with earlier stage disease

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Thank You

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